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Common
BLOOD AND
TISSUE
PARASITES
of Man

Life Cycle Charts

U. S. DEPARTMENT OF
HEALTH, EDUCATION, AND WELFARE
Public Health Service

Common BLOOD AND TISSUE PARASITES of Man

Life Cycle Charts

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COMMON BLOOD AND TISSUE PARASITES OF MAN



I. Introduction

The blood and tissue parasites of man include representatives of two groups of helminths, nematodes and cestodes, and of two groups of protozoa, hemoflagellates and sporozoa. In general, the life cycles tend to be more complex than those of the intestinal parasites and, in the case of the blood parasites, involve an arthropod vector as well as a human host. Intermediate hosts are necessary for the transmission of most of the blood and tissue organisms and in several cases, reservoir hosts are important. With the exception of *Toxocara canis*, no external development takes place.

Like those of the intestinal parasites,* the life cycle charts of the blood and tissue parasites are intended for use by students of parasitology, laboratory technicians, public health workers, and physicians. They are designed as simple, basic patterns that purposely omit details of epidemiology, incubation periods, patent periods, and exceptions to the usual pattern. The individual user can add any needed or desired details, obtaining this information from lectures or from the literature. *Toxoplasma gondii* has been excluded from this presentation since neither the correct classification nor the complete life history has been determined.

The design of the charts conforms to the following general rules, insofar as possible:

1. The diagnostic and infective stages are indicated and emphasized. These stages are in proportion with regard to species within a given group but, because of size variations, the scale is not uniform between groups. The sizes of the nematode male and female adults are relative to each other and, within the filariae, are drawn to a single scale.

*Melvin, D. M., Brooke, M. M. and Sadun, E. H. 1965. Common Intestinal Helminths of Man - Life Cycle Charts. PHS Publication No. 1235.

Brooke, M. M. and Melvin, D. M. 1964. Common Intestinal Protozoa of Man - Life Cycle Charts. PHS Publication No. 1140.

2. Morphological details are included in a diagrammatic fashion in most of the stages of the protozoa, but only in the diagnostic and infective stages of the helminths.
3. Survival times, pre-patent and patent periods, and developmental times are omitted.
4. Not all of the embryonic and larval stages of the helminths are indicated. For example, the number of nematode larval stages are not recorded.
5. Only broad groups of organisms are indicated as invertebrate intermediate hosts. More specific names are applied to mammalian hosts.
6. Reservoir hosts are not listed on the charts, but in cases where man is an accidental or abnormal host, the common hosts are indicated.
7. No general references are listed since the material incorporated into the charts is commonly found in most parasitology textbooks. However, where necessary, specific references have been included.

II. Blood Parasites

The blood parasites presented here include malaria, hemoflagellates, and filaria. Not all of the species of each group actually inhabit the blood stream (for example, adult filaria, *Leishmania* spp.) but most are associated with the circulatory system at some stage of their development. Possibly the leishmania might be considered as tissue rather than blood parasites, but since they are classified as hemoflagellates they are presented here with the blood inhabiting forms. Another tissue parasite is *Dracunculus medinensis* which is usually put in the same general category as the filariae, and is also included with the blood parasites in these charts.

Malaria

The life history of malaria is similar to that of the intestinal sporozoa, the coccidia, and involves an asexual cycle, schizogony, in the human host and a sexual cycle, sporogony, in the vector, a species of *Anopheles* mosquito. The pattern presented here is that of *Plasmodium vivax* but, in general, it is the same for all four species.

Immediately after the introduction of the infective sporozoites through the bite of the mosquito, a pre-erythrocytic (exo-erythrocytic) development occurs. In man, these exo-erythrocytic stages have been demonstrated in the parenchymal cells of the liver. On the basis of the knowledge of the prepatent period, this pre-erythrocytic phase probably requires a week or more depending on the species involved. In *P. vivax*, *Plasmodium ovale*, and *Plasmodium malariae* residual exo-erythrocytic stages probably continue in fixed cells during the erythrocytic phases, while in *Plasmodium falciparum*, on the other hand, residual exo-erythrocytic stages probably do not occur. The presence or absence of residual exo-erythrocytic stages affects both the clinical course and the therapy of the disease.

The asexual stages of malaria include trophozoites and schizonts and, except in *P. falciparum*, all stages of growth may be found in peripheral blood. *P. falciparum* organisms complete their schizogony in the capillaries of the internal organs so that usually only the rings (young trophozoites) of the asexual forms are seen in circulating blood.

In addition to the asexual stages, gametocytes (sexual forms) develop in man and in all four species, may be found in peripheral blood. Their exact origin is unknown. Some workers believe that they develop from certain of the merozoites produced in the erythrocytic schizonts; others, that they come from merozoites formed in

exo-erythrocytic schizogony. Gametocytes are the infective stages for the mosquito and, in the arthropod stomach, develop into gametes which initiate the sexual cycle. They do not multiply in the human host, and unless ingested by the appropriate mosquito, will degenerate and die within a few days. The sexual development, ending in production of sporozoites, the infective stage for man, is influenced by such extrinsic factors as temperature and humidity. The average length of both sexual and asexual cycles for each species is included in the table below. These are based on reports in the literature (by various investigators) and represent the more common average development periods as recorded.

The *Anopheles* species involved as hosts for human malaria vary with the geographical area. There are over sixty species which are considered vectors of malaria in different areas of the world. In the United States, there are only two that are considered to be important vectors: *A. quadrimaculatus* in the east and *A. freeborni* in the west. Not all species of *Anopheles* serve as malaria vectors, either because they are not good biological hosts, or because they normally do not feed on human blood.

Malaria infections can be spread from man to man via blood inoculations, for example, transfusions or common hypodermic needles used by drug addicts, but an exo-erythrocytic phase does not occur. Exo-erythrocytic development takes place only after sporozoite inoculation.

Man is considered to be the only natural vertebrate host for the four species of human malaria. However, recently it has been found that *P. cynomolgi*, a parasite of monkeys resembling *P. vivax*, can be transmitted by mosquitoes to humans (Eyles, *et al.*, 1960). While there is at present no clear-cut evidence that transmission occurs naturally, the possibility of monkey to man infection exists. Since this early report of Eyles, man to man transmission of *P. cynomolgi* by mosquitoes has been demonstrated by Contacos *et al.* (1962). The susceptibility of humans to simian malaria species may influence control and eradication programs in areas in which they are endemic.

References

- Eyles, D. E., Coatney, G. R., and Getz, M. 1960. Vivax-type malaria parasites of Macaques transmissible to man. *Science* 131:1812-1813.
- Contacos, P. G., Elder, H. A., Coatney, G. R., and Genter, C. 1962. Man to man transfer of *Plasmodium cynomolgi* by mosquito bite. *Am. J. Trop. Med. Hyg.* 11(2):186-193.

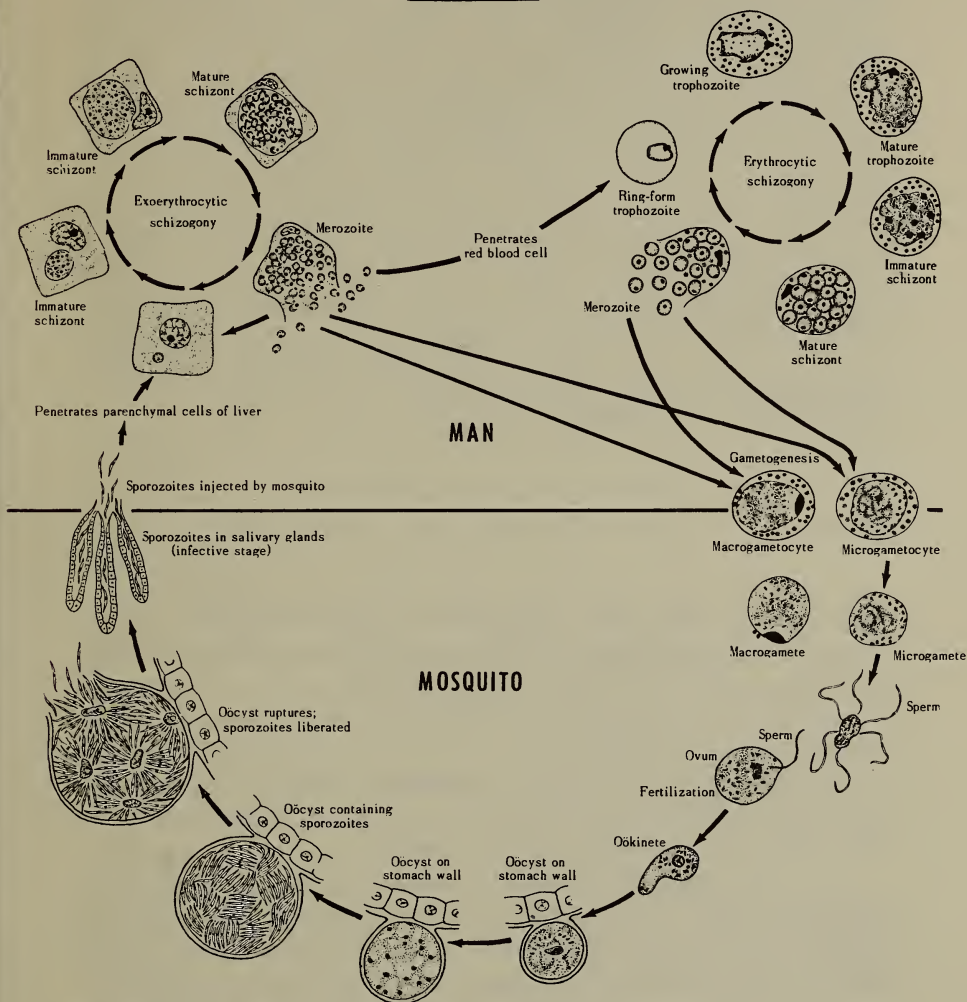
AVERAGE DEVELOPMENT TIMES*

	P. vivax	P. ovale	P. malariae	P. falciparum
Length of Pre-erythrocytic Phase	Approx. 8 days	Approx. 9 days	Approx. 12 days	Approx. 6-7 days
Length of Pre-patent Period	11-13 days	14-15 days	15-16 days	9-13 days
Length of Erythrocytic Asexual Cycle	42-48 hours	48-50 hours	72 hours	48 hours
Residual Exo-erythrocytic Phase	Present	Present	Present	Not present
Length of Sexual Cycle in Mosquito (Optimum conditions)	8-12 days	14-15 days	15-21 days	12-14 days

* Boyd, M. F. 1949. Malariology. W. B. Saunders Co., Philadelphia.
 Wilcox, A. 1960. Manual for the Microscopical Diagnosis of Malaria in Man.
 PHS Publication No. 796. Government Printing Office, Washington.

LIFE CYCLE of—

Malaria



Based on life cycle of *Plasmodium vivax*

Hemoflagellates

The life history patterns of the hemoflagellates, like that of malaria, involve an arthropod vector which is chiefly responsible for the transmission and spread of the infection. The vectors for the hemoflagellates are various species of flies, and the specificity of the vector usually limits the geographical distribution of the parasite.

Unlike most of the other blood parasites, the hemoflagellates do not possess sexual forms and multiplication occurs entirely through binary fission in one or more of the morphological stages. Species of two genera, *Trypanosoma* and *Leishmania* parasitize man. Four morphological stages are described: leishmania, leptomonas, crithidia, and trypanosome. Of the four, the leishmania are the only non-flagellated forms and both crithidial and trypanosomal stages possess an undulating membrane in addition to the flagellum. Except for *Trypanosoma cruzi*, no more than two of the four stages are associated with each genus of organisms.

Leishmania

In the human host, *Leishmania* spp. exist only in the leishmania form and are intracellular parasites of reticulo-endothelial cells: *L. donovani* predominantly in bone marrow and internal organs such as spleen and liver, *L. tropica* in skin and subcutaneous tissue, and *L. brasiliensis* in cutaneous and mucocutaneous tissues. Three other species of *Leishmania*, *L. peruana*, *L. guyanensis*, and *L. mexicana*, have been involved in cutaneous leishmaniasis in Peru, in Panama, and in Mexico, Guatemala, and British Honduras, respectively. The cycles of all species are similar.

In the arthropod vectors, which are certain species of *Phlebotomus* (sand-flies), the leishmania stages taken up during the insect bite transform into the leptomonas forms. These leptomonads divide in the midgut and in 3 to 5 days move to the proboscis of the sand-fly. When the insect feeds again, the leptomonads (infective forms) are injected into the vertebrate host where they again become leishmania within reticulo-endothelial cells.

Several species of *Phlebotomus* have been incriminated as vectors of leishmania, among them *P. argentipes* and *P. chinensis* for *L. donovani*, *P. intermedius* for *L. brasiliensis*, and *P. papatasi* and *P. sergenti* for *L. tropica*.

Dogs, rodents, and possibly other mammals may serve as reservoir hosts.

Trypanosomes

Three species of trypanosomes are known to infect man: *Trypanosoma gambiense* and *Trypanosoma rhodesiense*, etiologic agents of African sleeping sickness (African trypanosomiasis) and *Trypanosoma cruzi*, etiologic agent of Chagas' Disease (American trypanosomiasis). In addition to *T. cruzi*, a second species, *Trypanosoma rangeli*, has been reported from man and other animals in the western hemisphere but has not been included in the charts presented here.

The life cycles of the two African trypanosomes are similar except in the specific fly vector and are shown in a single chart. These forms occur in man only in the trypanosomal form and are ordinarily located in the blood stream and lymph nodes in the early phases of infection and in the central nervous system (primarily *T. gambiense*) in the chronic phases. They multiply in man by longitudinal binary fission of the trypanosomes.

In the arthropod vector, species of tsetse flies, the trypanosomes, taken up during the bite, multiply by binary fission in this stage in the midgut. They then migrate to the salivary glands where they become crithidial forms and undergo a second multiplication. In about 2 to 3 weeks they become metacyclic trypanosomes. These infective stage trypanosomes are introduced into the vertebrate host when the fly bites again.

The principal species of tsetse flies which serve as vectors for the two trypanosome species are *Glossina palpalis* and its subspecies, *G. palpalis fuscipes* and *G. tachinoides* for *T. gambiense* and *G. morsitans*, *G. pallidipes* and *G. swynnertoni* for *T. rhodesiense*. The choice of specific vectors determines to a degree the geographical distribution of the trypanosome infections: *T. gambiense* is found chiefly in tropical West and Central Africa and *T. rhodesiense* in northeastern and southern Rhodesia, Nyasaland, Portuguese East Africa, Tanganyika, and Eastern Uganda.

Wild game mammals such as antelope, probably are reservoir hosts for *T. rhodesiense*, and cattle, hogs, and goats may possibly serve as reservoir hosts for *T. gambiense*, although this has not been definitely established.

The life cycle of *T. cruzi* is markedly different from that of the African trypanosomes. In the mammalian host, two forms, the trypanosome and leishmania stages, may be found. The trypanosome form usually occurs in the blood stream during the early acute phase and during febrile periods. The leishmania stage is found in the tissue, usually either reticulo-endothelial cells or heart muscle cells. Occasionally, they are found within macrophages in the blood. In the vertebrate host, the parasite divides only in the leishmania stage.

The vector, a species of triatomid bug, may ingest the typanosome stage in the blood or the leishmania stage within a macrophage during feeding. In the bug midgut the parasite becomes the flagellated crithidial form and multiplies. The organisms then migrate to the hindgut where they become metacyclic or infective trypanosomes. These forms passed in the feces discharged as the bug feeds, ordinarily enter the mammalian host by being rubbed into the bite wound.

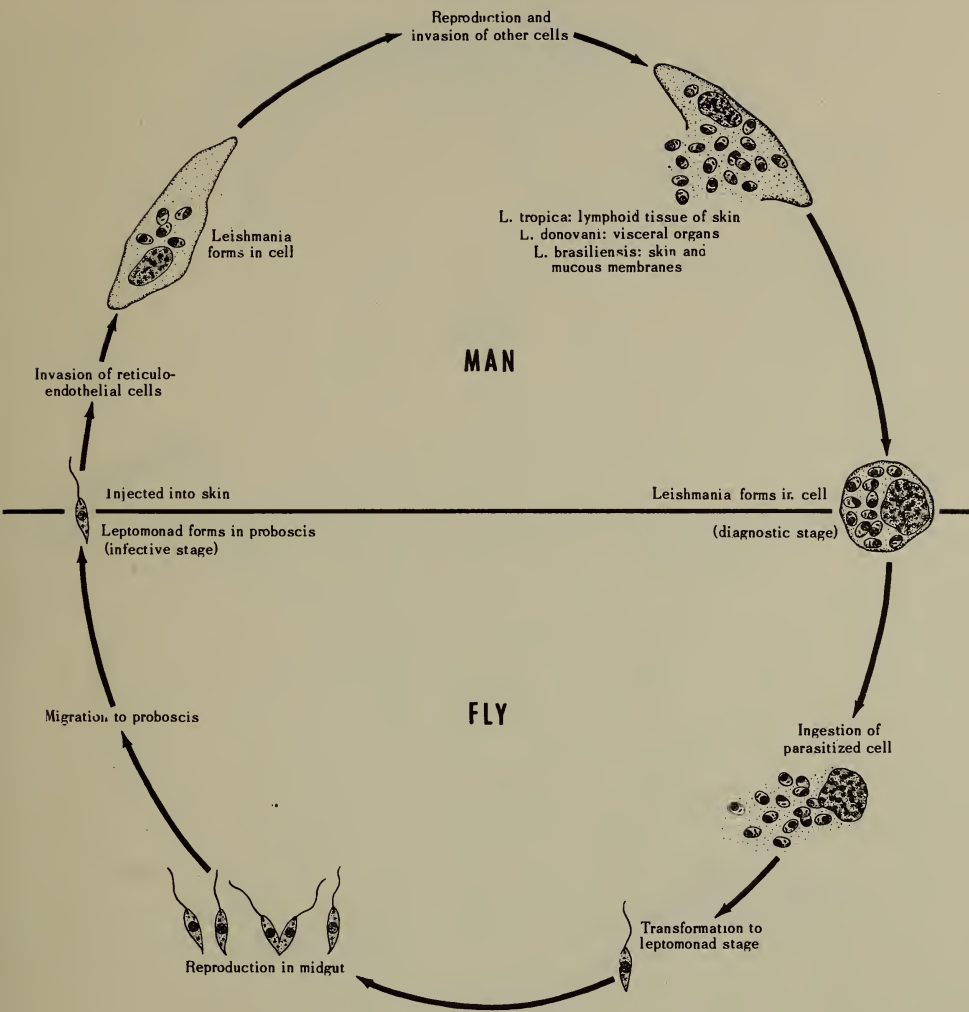
The triatomid species incriminated as vectors are *Panstrongylus megistus*, *Triatoma infestans* (southern South America), *T. dimidiata* (Central America) and *Rhodnius prolixus* (northern South America and Central America).

Both domestic and wild mammals serve as reservoir hosts including dogs, cats, pigs, armadillos, and rodents among others.

The second American species, *T. rangeli*, morphologically is more nearly like the African trypanosomes than like *T. cruzi*. However, in its choice of a vector, a genus of triatomid bugs, it resembles the latter. The life cycle differs from that of *T. cruzi* in the following aspects: the metacyclic trypanosomes in the vector gain access to the vertebrate host through the bite of the bug as well as through fecal contamination of the bite wound as occurs in *T. cruzi*; no leishmania stages have been found in the vertebrate host. *T. rangeli* has been reported from northern South America and from Central America.

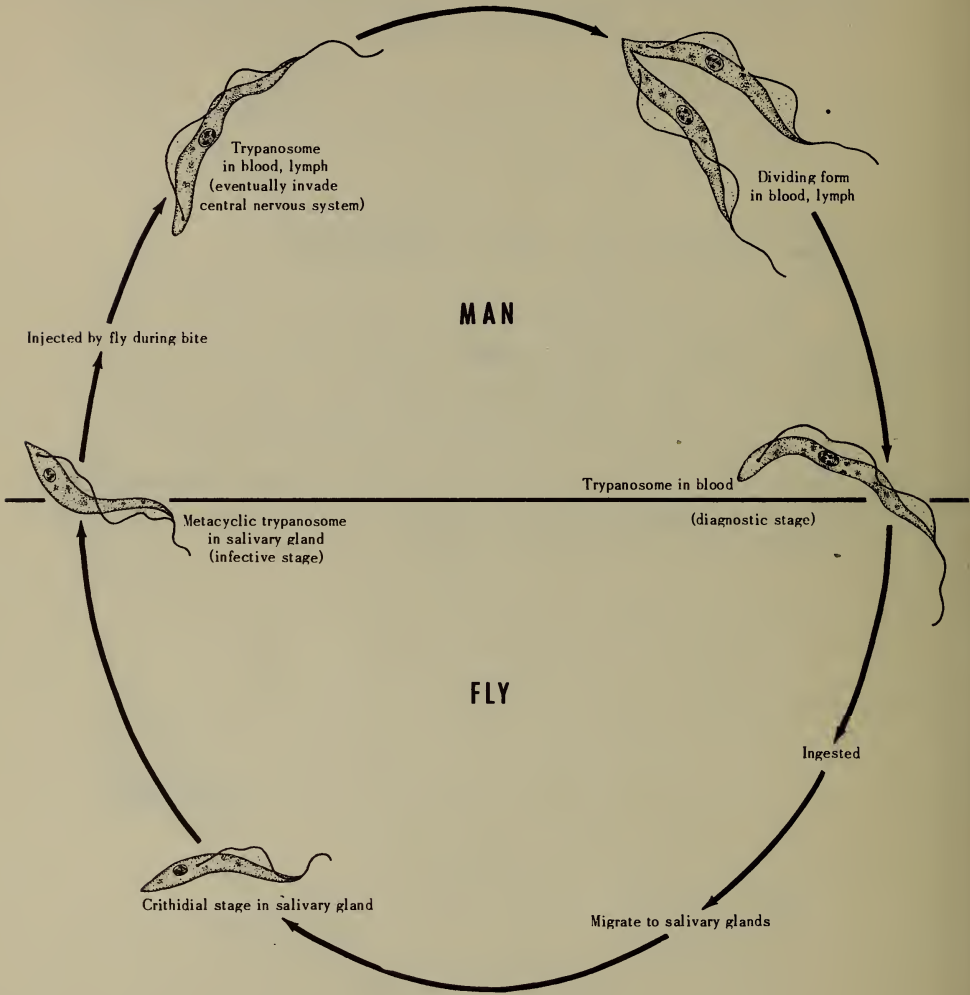
LIFE CYCLE of—

Leishmania



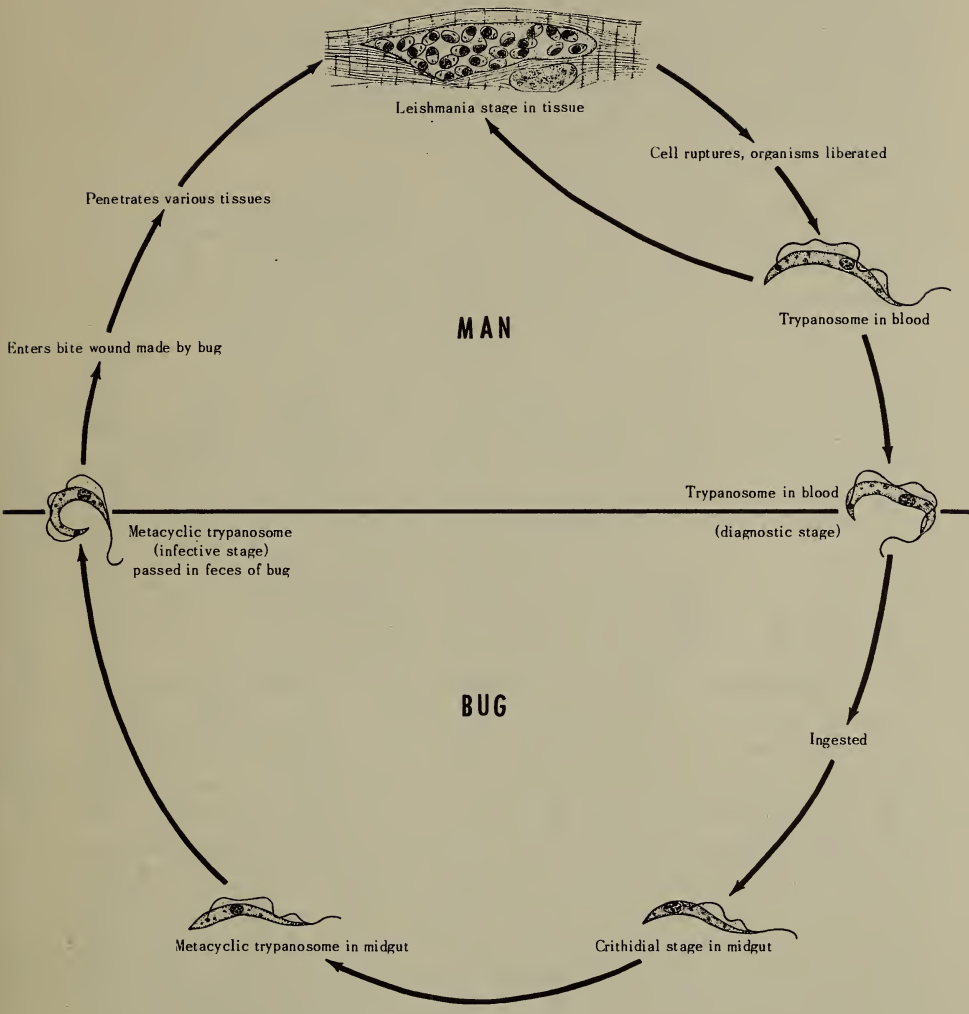
LIFE CYCLE of—

Trypanosoma gambiense and *T. rhodesiense*



LIFE CYCLE of—

Trypanosoma cruzi



Filaria

The life histories of the various species of human filaria are similar except for the specific arthropod host and the location of the adults within the human body. These blood nematodes differ from the intestinal species in that the diagnostic stage is a prelarval form called a microfilaria and there is no external environment period. Most of the structural details have been included in the drawings of the microfilariae but other stages are more diagrammatic. Within the group, the diagnostic and infective stages have been drawn to scale, and to a lesser degree, the adults.

Like other helminths, filariae do not multiply in man. Furthermore, passage through the arthropod host is necessary for transmission of the infection. For example, microfilariae in transfused blood will circulate in the peripheral blood of the recipient but are unable to cause infection and will die within a relatively short time.

Within the human host, the worms mature slowly requiring several months to a year before diagnostic stages (microfilariae) can be demonstrated. The location of adults varies with the species (see table below) but microfilariae are found in the peripheral blood in all species except *Onchocerca volvulus* where they are present in the cutaneous tissues. The appearance of microfilariae in the blood is periodic in certain species (*Wuchereria bancrofti*, *Brugia malayi*, and *Loa loa*) and non-periodic in others (*Acanthocheilonema perstans*, *Mansonella ozzardi*, and the South Pacific strain of *W. bancrofti*). The reasons for this periodicity are not clearly understood.

The arthropod host may be a species of mosquito (*W. bancrofti* and *B. malayi*), of flies (*O. volvulus* and *L. loa*), or biting midges (*A. perstans* and *M. ozzardi*). There is no multiplication of the filariae within the vector as occurs with the blood protozoa. The ingested microfilariae penetrate the stomach wall of the insect after losing the sheath if one is present and develop to the infective third stage larvae in the thoracic muscles. The infective larvae then migrate to the proboscis, and when the insect bites again, they actively move down the proboscis to the skin surface and probably enter the human host through the bite wound. The development within the insect is influenced by such extrinsic factors as temperature and humidity.

The average developmental time and some of the chief vectors for each species are included in the table below.

While several species of arthropods may be involved as intermediate hosts for the filariae, man is the usual definitive host in most instances. *A. perstans* has been reported in the gorilla, *L. loa* in the baboon (although their role as reservoir host is yet to be proved) and, recently, *B. malayi* has been recovered from cats and monkeys. Of the six species, *A. perstans* and *M. ozzardi* are the only ones usually considered non-pathogenic, although the possible pathogenicity of *A. perstans* has recently been suggested.

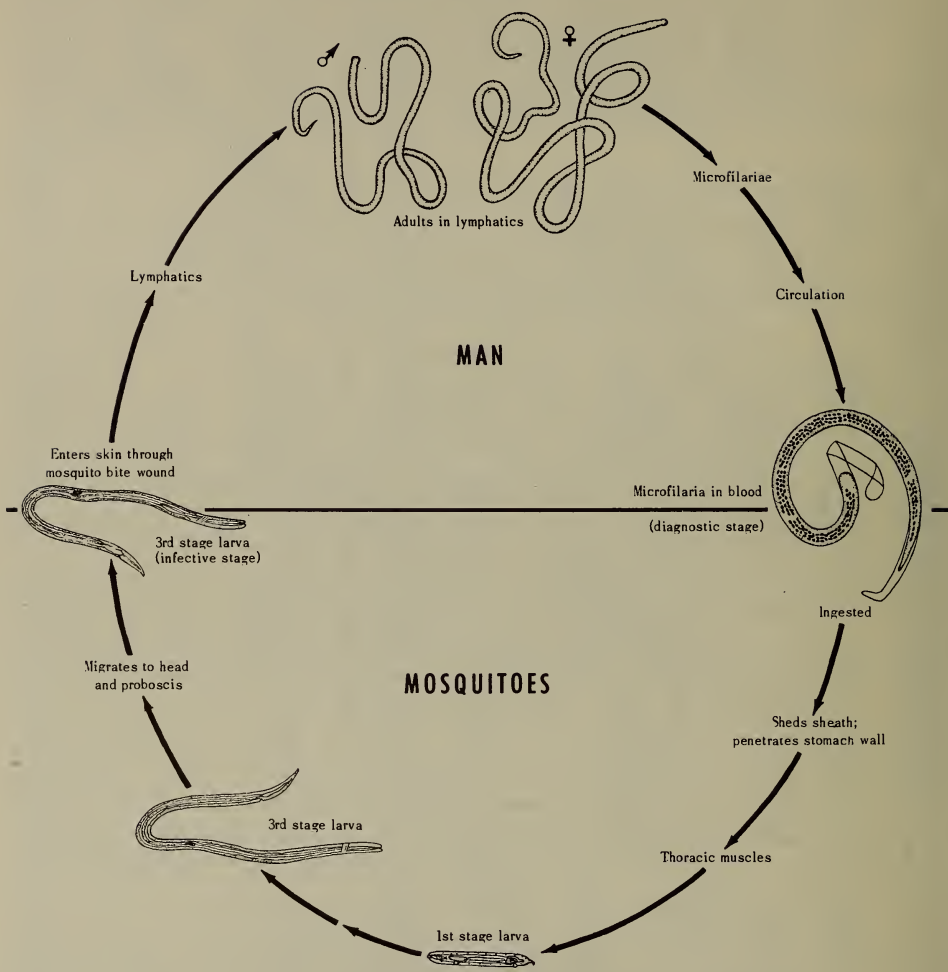
CHARACTERISTICS OF FILARIAE

	<i>W. bancrofti</i>	<i>B. malayi</i>	<i>L. loa</i>	<i>M. ozzardi</i>	<i>A. perstans</i>	<i>O. volvulus</i>
Geographical Distribution	Tropical and subtropical areas 41°N - 28°S	East Indies, Southern Asia	Africa	South and Central America	Africa, South America	Africa, Central and South America
Arthropod Host	Mosquitoes: <i>Culex quinquefasciatus</i> , <i>Aedes polynesiensis</i>	Mosquitoes: <i>Mansonia</i> sp.	Tabanid flies: <i>Chrysops dimidiata</i> , <i>C. silacea</i>	Midges: <i>Culicoides furens</i>	Midges: <i>Culicoides austeni</i> , <i>C. grahami</i>	Black flies: <i>Simulium damnosum</i> , other <i>Simulium</i> sp.
Developmental Times: Arthropod Man	14-15 days approx. 1 year or more	6-7 days approx. 1 year	10-12 days approx. 1 year	7-9 days approx. 1 year	7-9 days approx. 1 year	8-9 days approx. 1 year or less
Location in man: Adults	Lymphatics	Lymphatics	Subcutaneous tissue	Mesentery, body cavities	Mesentery, perirenal and retroperitoneal tissue Blood	Subcutaneous tissues
Microfilariae	Blood	Blood	Blood	Blood		Skin, subcutaneous tissues
Periodicity of Microfilariae	Nocturnal	Nocturnal	Diurnal	Non-periodic	Non-periodic	Non-periodic

* A second species of *Acanthocheiloneima*, *A. streptocerca*, whose microfilariae are found in subcutaneous tissue rather than blood, has been reported from man but is not included here.

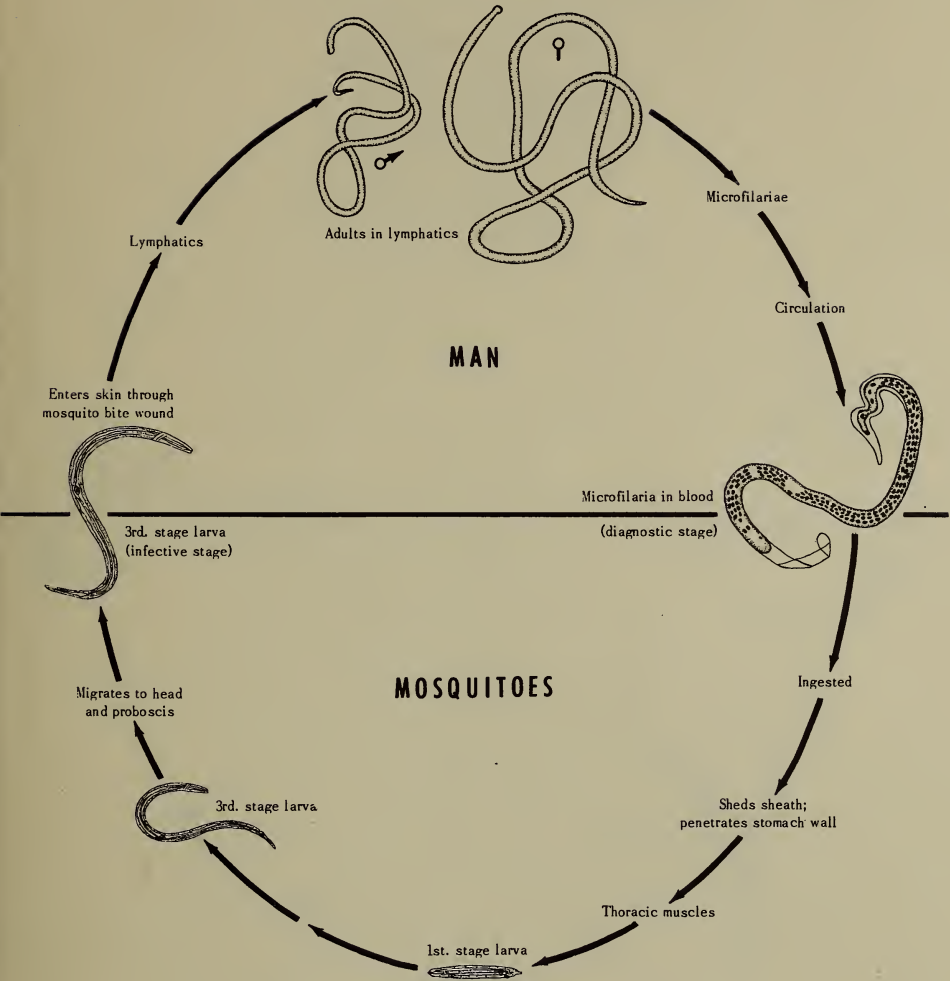
LIFE CYCLE of—

Wuchereria bancrofti



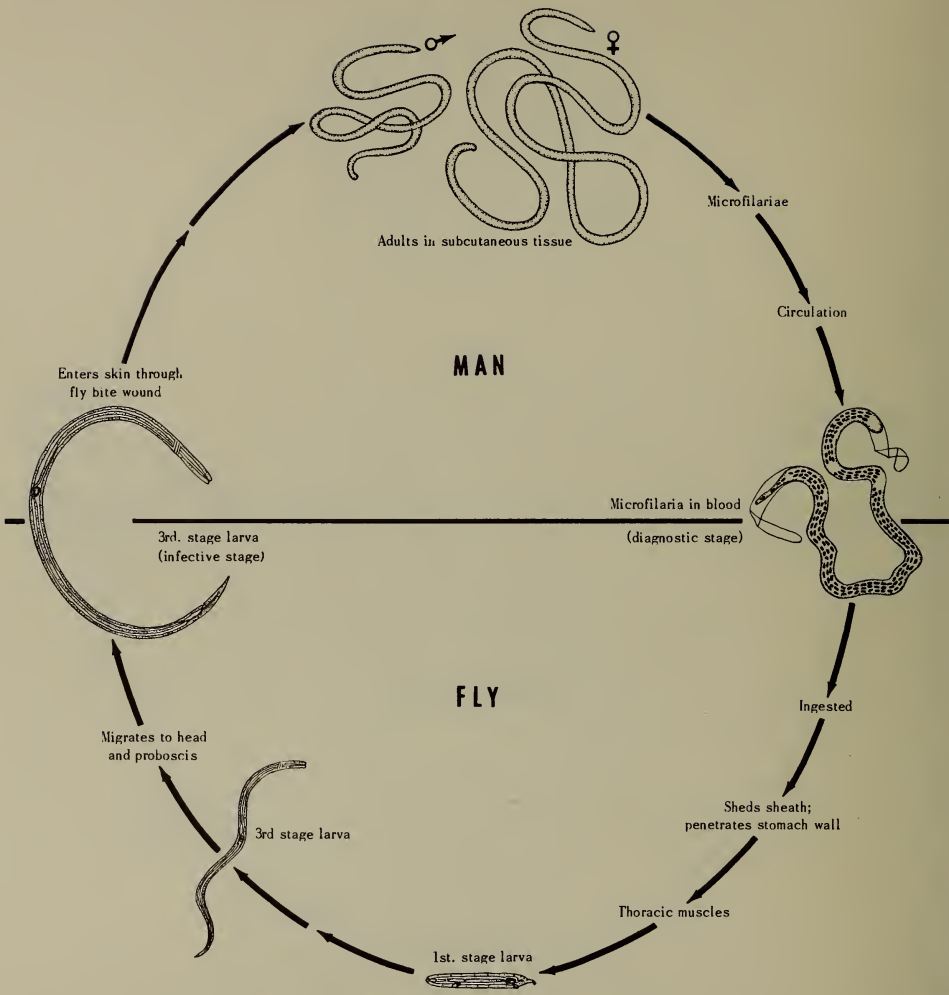
LIFE CYCLE of—

Brugia malayi



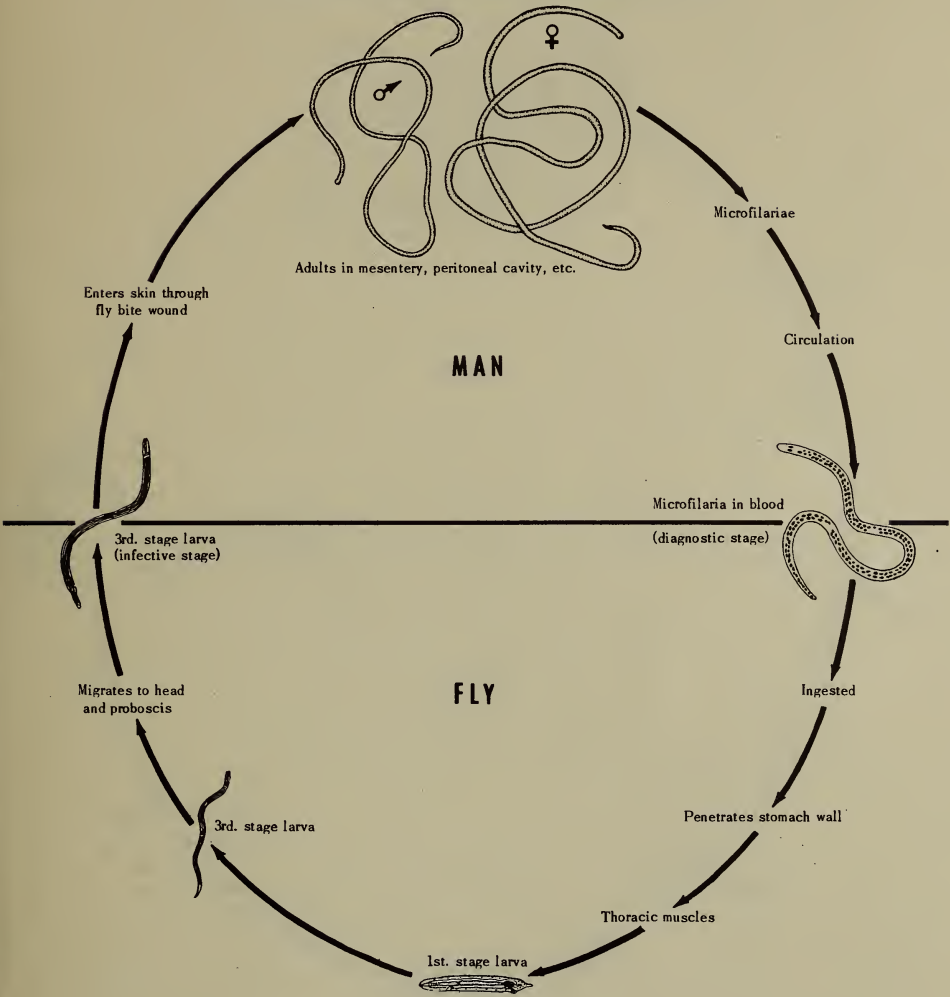
LIFE CYCLE of—

Loa loa



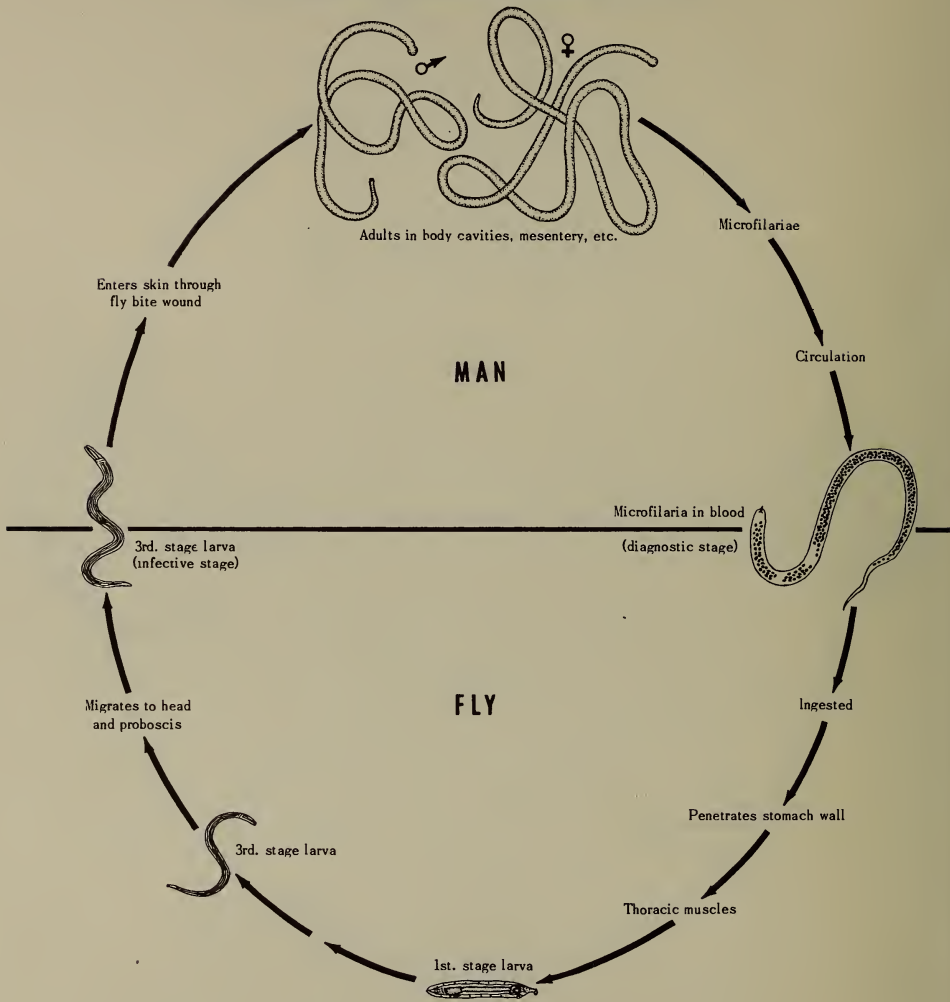
LIFE CYCLE of—

Acanthocheilonema perstans



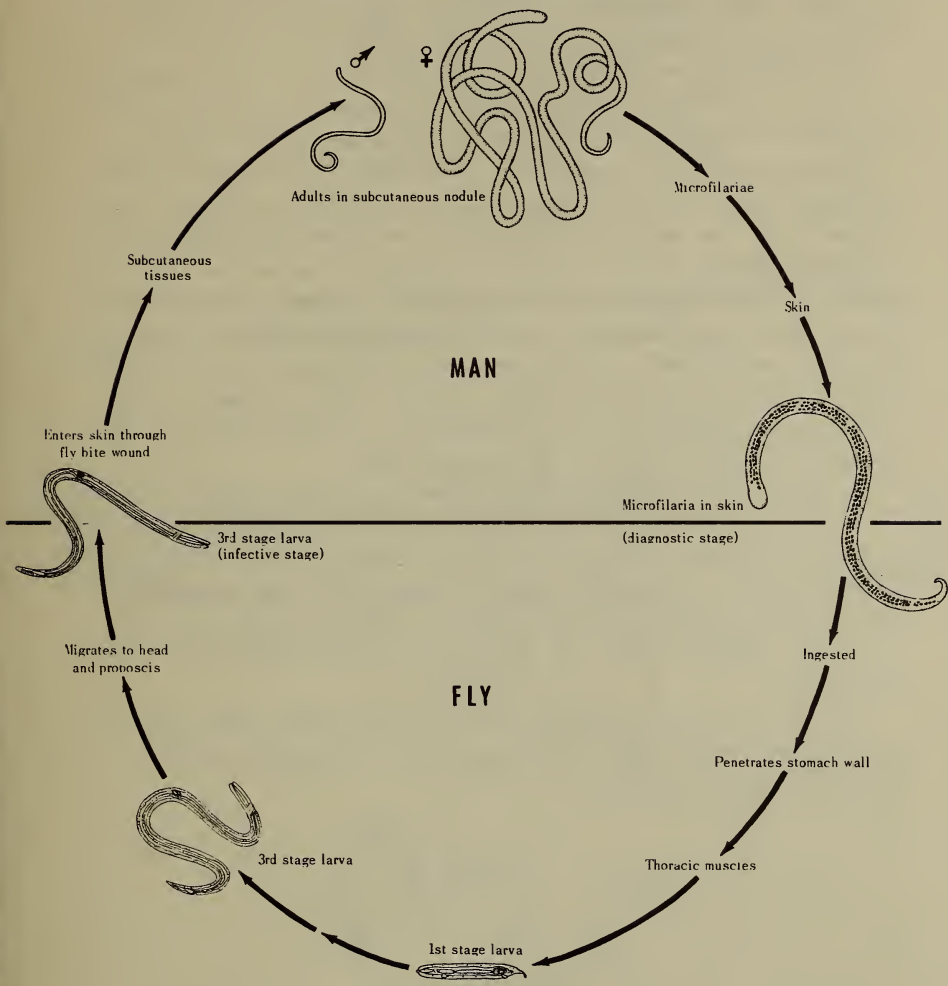
LIFE CYCLE of—

Mansonella ozzardi



LIFE CYCLE of —

Onchocerca volvulus



Dracunculus

Dracunculus medinensis is often grouped with the filariae, but since the life cycle differs significantly it is discussed separately. The diagnostic and infective stages, however, are drawn in proportion to those of the filariae. The sizes of the adult *Dracunculus* worms are relative to each other but not to filariae adults.

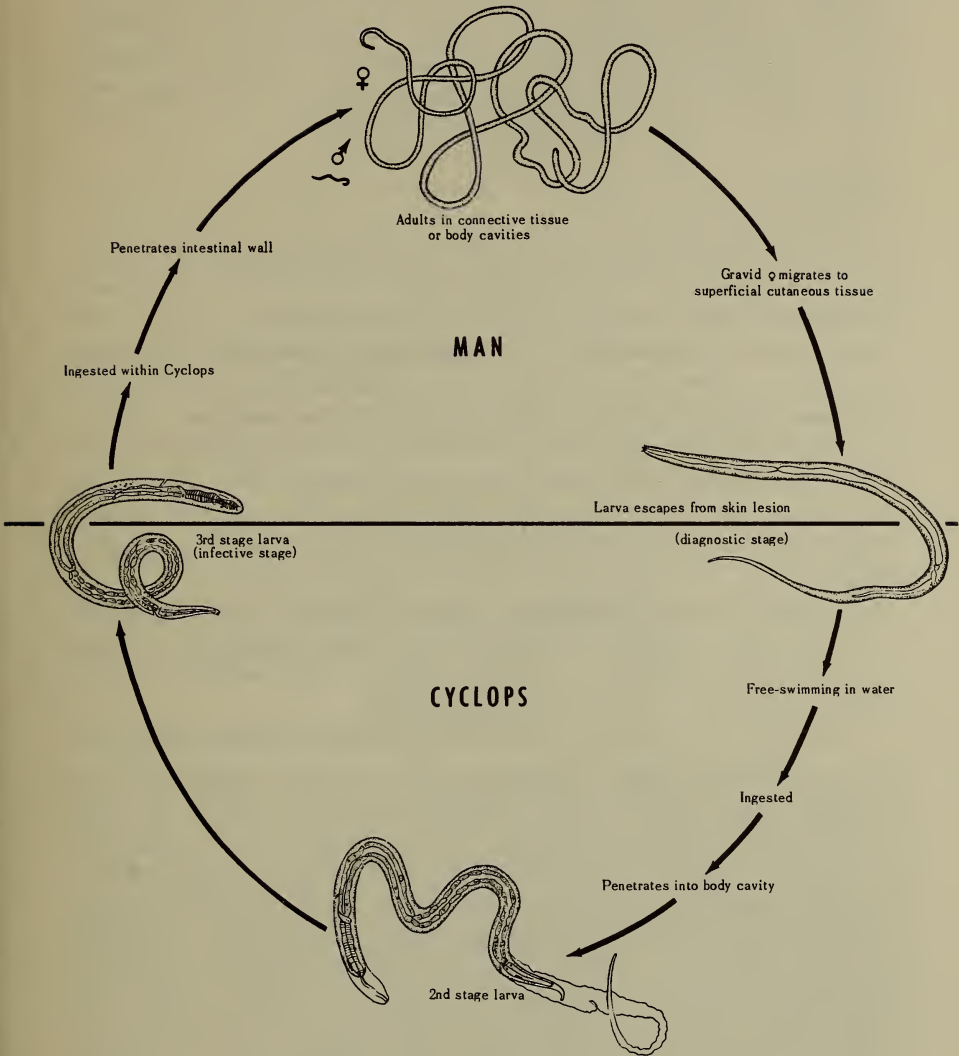
D. medinensis, or the guinea worm, is probably the "fiery serpent" referred to in biblical writings and is a parasite of man in Africa, southwestern Asia, northeastern South America and West Indies.

Man acquires infections with *Dracunculus* by ingestion of the arthropod host containing infective larvae, rather than by bite of the vector as is true of most of the other blood parasites. After slowly maturing in the loose connective tissue or serous cavities, the gravid female migrates to the superficial cutaneous tissue. First stage larvae are liberated from the female worm directly into the external environment, in this case into water, through an ulcer or blister which forms on the skin over the worm's vaginal opening. The free-swimming larvae are ingested by a species of *Cyclops* and mature in the body cavity in about three weeks.

In many respects, *Dracunculus* differs from other blood and tissue parasites. While it requires an intermediate host for completion of its life cycle like the filariae, its choice of host (a crustacean rather than a species of *Diptera*), mode of entry into both arthropod and human (by ingestion), and the existence of free-swimming larvae are markedly different from the patterns of other blood and tissue parasites.

Man is not the only definitive host of *Dracunculus*. Both domestic and wild animals — dogs, cats, foxes, mink, even horses and cattle — have been reported infected.

Dracunculus medinensis



III. Tissue Parasites

The three species of helminths included here inhabit human body tissues in the larval form. The adults of all three are normally inhabitants of the intestine of the definitive host. Man may be an intermediate host (*Echinococcus*) or both intermediate and definitive hosts (*Trichinella*) or simply an accidental host (*Toxocara*). In all three charts, the cycle in man has been left unclosed to denote the "blind alley" ending of the parasites in humans.

Trichinella spiralis

T. spiralis is a nematode parasite which goes through both adults and larval stages within a single animal host but two hosts are necessary to continue the infection. Except in the tropics, it is world-wide in distribution. The cycle is a relatively simple one with a short adult life span and a considerable longer larval life. The host, which is both the definitive and intermediate host, may be any carnivorous or omnivorous animal, but chiefly, man, hogs, rats, bears, foxes, dogs, and cats. From the standpoint of man, the hog is the primary source of infection, and the life cycle chart has been prepared on this basis, including only the most important and basic steps.

It is the general consensus, that the infection is maintained in swine primarily through ingestion of the infective larvae in meat scraps (usually pork) in uncooked garbage. This swine to swine transmission is shown in the life cycle chart.

The cycle in man is initiated by ingestion of meat (pork) containing encysted larvae (diagnostic and infective stages). In the intestine the liberated larvae mature very rapidly and by the fifth day the females begin to deposit larvae, a process which continues for about 4 weeks or longer. The males live for a relatively short time and usually are passed out soon after fertilization. The young larvae reach the tissues by way of the lymphatics and blood. Although they are carried to all parts of the body, they ordinarily develop only in striated muscle. Encystment may begin at about 3 weeks and calcification of the cyst often starts as early as 6 months and is usually completed within 18 months. The majority of the encysted larvae probably die within 1 to 2 years after infection.

Toxocara canis (Larva migrans)

Human infections with larvae of nematode parasites of lower animals are called larva migrans. Larva migrans may be caused by many different species of parasites and may be either cutaneous or

visceral depending on the body area affected and the parasite species concerned. Cutaneous larva migrans is commonly due to filariform larvae of the dog and cat hookworms. The cycle in the normal hosts is the same as that for human hookworms (included in the intestinal helminth series). In man the larvae are unable to proceed further than the cutaneous layers in the region of penetration. The principal agent of visceral larva migrans appears to be the dog ascarid, *Toxocara canis*. The life cycle of *T. canis* is included here as representative of the larva migrans group.

T. canis is an intestinal nematode having a life cycle similar to *Ascaris lumbricoides*, the human ascarid species. It is cosmopolitan in distribution. The one-celled egg (diagnostic stage) is passed in the feces of the dog and undergoes development in the external environment to the embryonated stage (infective stage). Upon ingestion by the normal host, these embryonated eggs hatch in the intestine and the liberated larvae undergo a lung migration before maturing in the lumen of the intestine.

Man becomes an accidental and abnormal host through ingestion of the embryonated eggs. In the human intestine, the eggs hatch and the larvae penetrate into the mucosa and the circulation. However, since they are not in a normal host they do not complete the lung migration but rather are filtered out in various organs, chiefly the liver. They remain immature and eventually die in the tissues. The infection is more common in children than in adults and is characterized by a persistent high eosinophilia.

Echinococcus granulosus

Echinococcus spp. (*E. granulosus* and *E. multilocularis*) are the etiologic agents of hydatid disease in man. *E. granulosus* is widely distributed in temperate and subtropical regions and other areas where sheep, cattle, and hogs are raised. *E. multilocularis* is prevalent in southern Europe, Russia, Alaska and neighboring territories. Only the larval stages infect humans and the hydatid cysts may be found in various tissue, chiefly liver and lungs. Like most cestodes, the normal life cycle of *Echinococcus* involves two hosts, definitive and intermediate. The adults are found in the intestines of various carnivora, especially dogs and foxes, and larval development occurs in sheep, cattle or swine (*E. granulosus*) or in rodents (*E. multilocularis*). The life histories of the two species are similar (except for the choice of intermediate host) so only that of *E. granulosus* is represented here.

The eggs of the worm (diagnostic stage) are passed in the feces of the definitive host. These are ingested by the intermediate host in which the infective larvae (hydatid cysts) develop. The larval

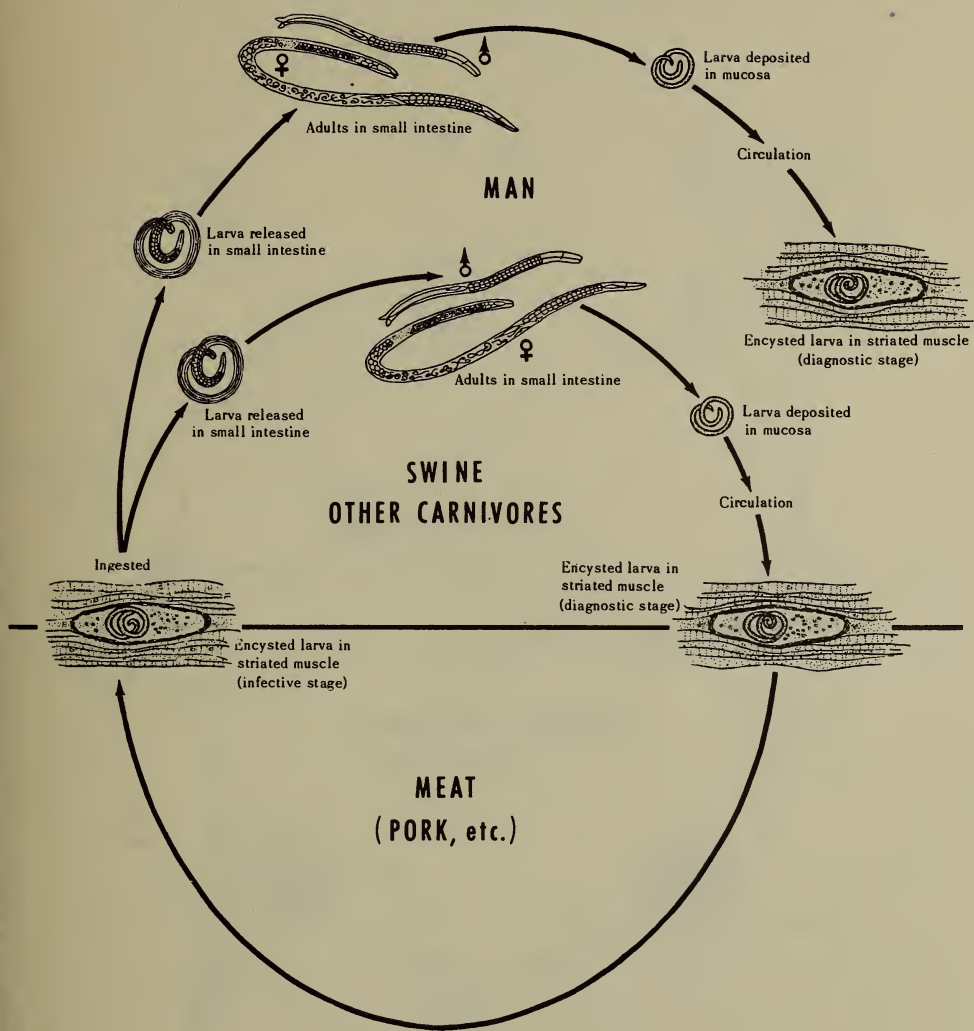
growth usually requires about 5 months. These larval forms differ from those of other human cestode infections in that multiple rather than single scoleces develop within the cyst. When hydatid cysts containing the scoleces are ingested by carnivora, adult worms mature in the small intestine in about 7 weeks.

Man may become an accidental intermediate host by ingestion of the eggs from contact with contaminated food, drink, or other materials.

In addition to *Echinococcus* larvae, man may also become the intermediate host of the larval stages of *Taenia solium* which in the adult stage normally infects the human intestine. The extra-intestinal phase of the *T. solium* cycle in man has been presented in the chart included with the intestinal helminths and is not repeated here.

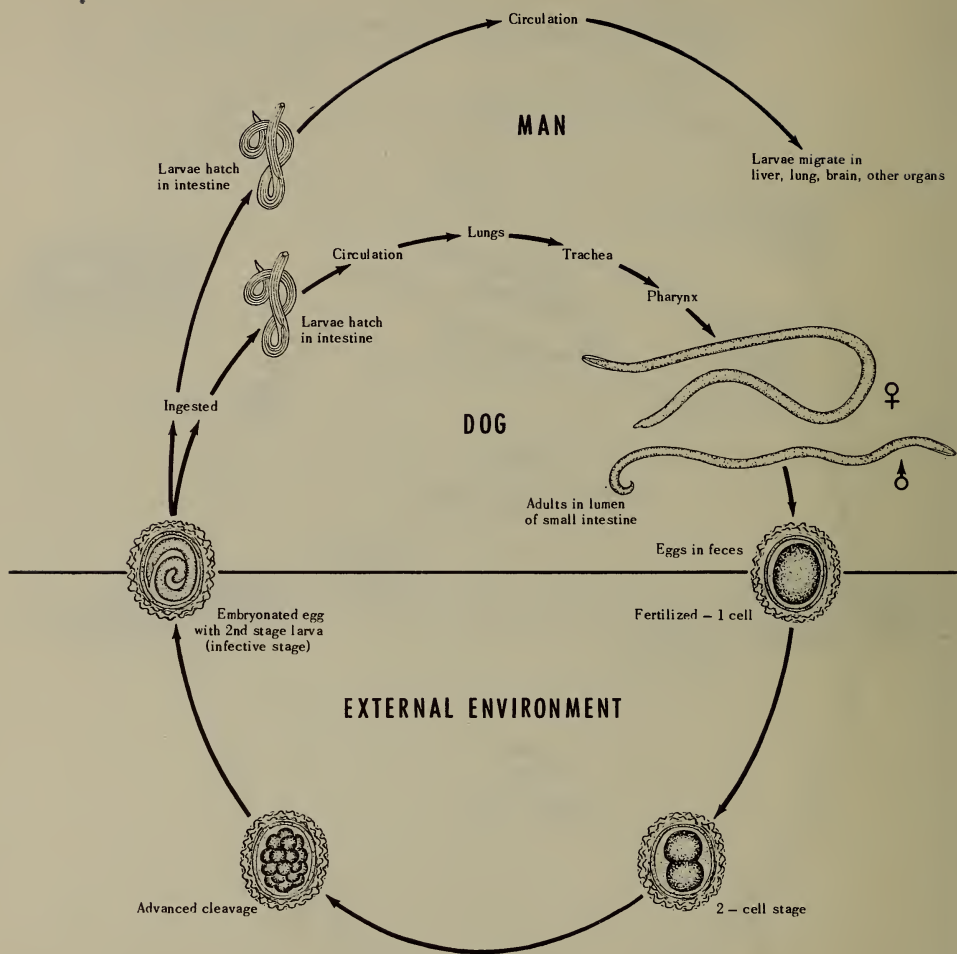
LIFE CYCLE of—

Trichinella spiralis



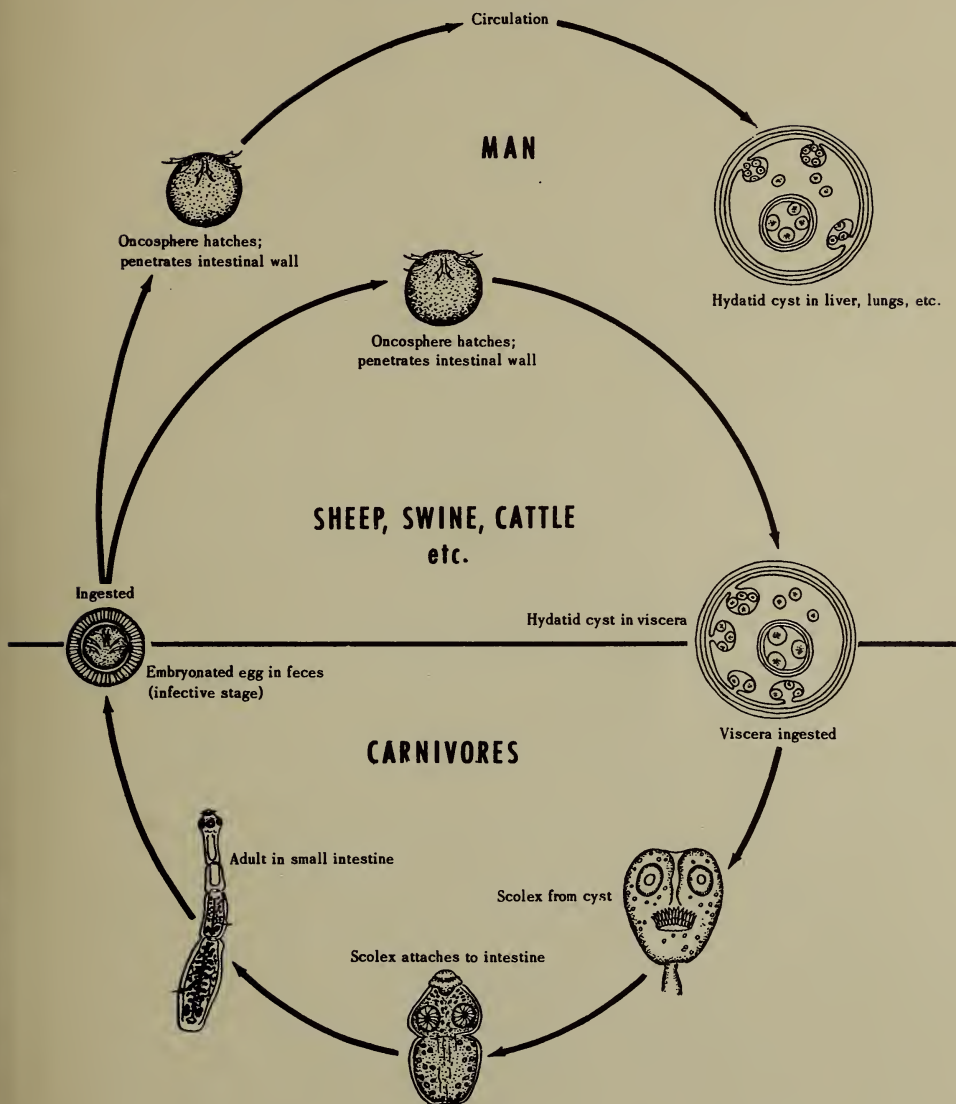
LIFE CYCLE of—

Toxocara canis



LIFE CYCLE of—

Echinococcus granulosus



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